Sealing of pulmonary arteries with LigaSure: In vivo and ex vivo examinations

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Objective: The LigaSure device has been demonstrated to be safe for systemic vessels up to 7 mm in diameter, although its use in thoracic surgery remains understudied. We aimed to evaluate the safety of LigaSure for pulmonary artery sealing.

Methods: In 30 cases of open lung lobectomy, 15 small pulmonary arteries (diameter, 3-5 mm) and 15 thick pulmonary arteries (diameter, 6-8 mm) were divided with LigaSure. Before closure of the thoracotomy, the vessel stumps were ligated proximal to the sealing zone, resected, and preserved in formaldehyde for histopathologic examination. In a control group, a similar number and size of pulmonary arteries were suture-ligated. The burst pressure of the pulmonary arteries from the resected lung lobes was measured.

Results: The mean burst pressure of small pulmonary arteries was 4.3-fold less after sealing than after ligation (315 ± 213.1 mm Hg vs 1345 ± 256 mm Hg; $P < .001$), and 6.4-fold less than after ligation of thick pulmonary arteries (156 ± 42.5 mm Hg vs 1007 ± 141.6 mm Hg; $P < .001$). Sealed pulmonary arteries >5 mm in diameter have a burst pressure that is 50% less than that of smaller arteries ($P < .001$). In all cases after sealing, the histologic examination demonstrated only a fusion of the adventitia, whereas the intima and media were replaced and invaginated into the vessel lumen.

Conclusions: LigaSure does not result in complete fusion of the wall layers of pulmonary arteries. The pulmonary artery burst pressure after sealing is significantly less compared with conventional suture ligation. It remains unclear whether these findings create a clinical risk of rupture. (J Thorac Cardiovasc Surg 2013;145:1525-8)

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Videothoracoscopic lobectomy is an alternative to open lobectomy in early stages of nonsmall cell lung cancer.[1-3] The closure of pulmonary arteries by the videothoracoscopic technique must be as safe as the standard open procedure, particularly because hemorrhage resulting from insufficient closure of the pulmonary artery is a life-threatening complication. However, suture ligation of the pulmonary arteries is difficult through thoracoscopic ports, and the safest endoscopic procedure seems to be staple closure of the pulmonary arteries. Sometimes, left upper segmental branches in the fissure are difficult to divide using the really large, rigid endostapler.[4] This technique is expensive and time-consuming because several reloadable cartridges must be used, especially for upper lobectomies. LigaSure (Covidien, Neustadt/Donau, Germany), which is a bipolar vessel sealing device, could be an alternative to stapling. The aim of this study was to evaluate the safety of the LigaSure device for pulmonary artery closure.

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METHODS

From June 2011 to March 2012 we used the LigaSure vessel-sealing system on pulmonary arteries in 30 patients (male, n = 18; female, n = 12; average age, 67 years) undergoing open lung lobectomy. The study was approved by the ethics committee of the medical association of Thuringia. Written informed consent was obtained from all patients. Our study was divided into 2 experimental steps: in vivo experiments and ex vivo burst pressure measurement.

In Vivo Experiments

In 30 cases of open lung lobectomy (32 resected lobes, 2 bilobectomies) resulting from lung cancer, 15 small pulmonary arteries (diameter, 3-5 mm) and 15 thick pulmonary arteries (diameter, 6-8 mm) were divided with the LigaSure vessel-sealing system (LigaSure–pulmonary artery [LS-PA] group). The diameter of each pulmonary artery was measured with a sliding caliper in situ. All pulmonary arteries were sealed and divided with a LigaSure Blunt-Tip Laparoscopic Sealer/Divider (5 mm; LF 1537; Covidien, Neustadt/Donau, Germany) with the ForceTriad energy platform (Valleylab, Tyco Healthcare, Boulder, Colo) using an intensity setting of 2 bars. During lymphadenectomy, the remaining lobe was ventilated. Before closure of the thoracotomy, the vessel stumps were ligated proximal to the sealing zone, resected, and preserved in formaldehyde for histopathologic examination. All 30 sealed vessels were examined histopathologically.

A control group was also established, consisting of 30 cases of open lung lobectomy (31 resected lobes, 3 bilobectomies) for lung cancer (suture-ligated–pulmonary artery [L-PA] group). Compared with the LigaSure group, the control group had the same number and diameter of pulmonary arteries ligated, although it was done conventionally with 2-0 polyester suture.

Ex Vivo Burst Pressure Measurement

Both ligated and sealed pulmonary arteries from the resected lung lobes were dissected ex vivo immediately after resection. All peripheral

Abbreviations and Acronyms
L-PA = suture-ligated–pulmonary artery
LS-PA = LigaSure–pulmonary artery

branches of both ligated and sealed pulmonary arteries were suture-ligated except for 1 vessel branch that was preserved for introduction of a blunt cannula. The blunt cannula was secured with a ligation. Over a 3-way stopcock, the cannula was connected with an injection system and a digital pressure monitor (Freescale Semiconductor Inc, Austin, Tex). Saline was injected into the vessel lumen at a constant rate, increasing pressure by 1 mm Hg/second. The burst pressure was identified and recorded at the moment that the closed vessel ruptured (Figure 1).

Statistical Analysis

The following 4 groups were analyzed: (1) LS-PA 3-5, with sealed pulmonary arteries of 3-5 mm in diameter (n = 15); (2) LS-PA 6-8, with sealed pulmonary arteries of 6-8 mm in diameter (n = 15); (3) L-PA 3-5, with suture-ligated pulmonary arteries of 3-5 mm in diameter (n = 15); and (4) L-PA 6-8, with suture-ligated pulmonary arteries of 6-8 mm in diameter (n = 15).

The Mann-Whitney *U* test was used to compare the mean burst pressures of similar-size pulmonary arteries of the different closure techniques (LS-PA and L-PA). In addition, the burst pressures of the small and thick pulmonary arteries were compared among each closure technique. A 2-sided P value $\leq .05$ was considered a statistically significant difference between the groups. The statistical analysis was performed using IBM SPSS Statistics 20 (SPSS Inc, Chicago, Ill).

RESULTS

Characteristics of the 60 patients are shown in Table 1. In no case did an intraoperative hemorrhage occur. Sealed pulmonary arteries were left closed in vivo for a mean period of 32 minutes (range, 28-36 minutes). During this time, the remaining lobe was ventilated.

The burst pressures of sealed and ligated pulmonary arteries with different diameters are shown in Figure 2. The mean burst pressure was 4.3-fold lower after sealing than after ligation of small pulmonary arteries (315 ± 213.1 mm Hg vs 1345 ± 256 mm Hg; $P < .001$). Moreover, the mean burst pressure was 6.4-fold lower after sealing than after ligation of thick pulmonary arteries (156 ± 42.5 mm Hg vs 1007 ± 141.6 mm Hg; $P < .001$). Sealed pulmonary arteries >5 mm in diameter had a burst pressure that was 50% less than that of smaller arteries (156 ± 42.5 mm Hg vs 315 ± 213.1 mm Hg; $P < .001$). Ligated pulmonary arteries >5 mm in diameter also had a burst pressure significantly less than that of smaller arteries (1345 ± 256 mm Hg vs 1007 ± 141.6 mm Hg; $P = .001$).

In all 30 cases, the histologic examination showed an incomplete fusion of the wall layers after sealing. The histology clearly demonstrates that only the adventitia was sealed, whereas the intima and media were replaced and invaginated into the vessel lumen (Figure 3).

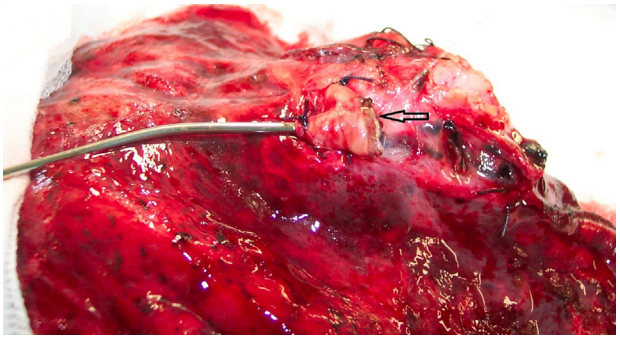

FIGURE 1. Burst pressure measurement. A blunt cannula is introduced into a stump of the pulmonary artery sealed by LigaSure. The water beam demonstrates a bursting of the sealed zone at a pressure of 158 mm Hg (*arrow*).

DISCUSSION

The closure of pulmonary arteries must be durable and safe; otherwise, life-threatening hemorrhage may occur. Historically, the pulmonary arteries have usually been ligated with a suture. However, suture ligation by videothoracoscopic lobectomy is technically fastidious, given that the operation is performed with thoracoscopic instruments through only 3-4 thoracoports. In addition, making a knot with endoscopic instruments is particularly dangerous because of the vulnerability of the pulmonary vessels. Therefore, alternative techniques have been used, such as the vascular stapler or clip.[5,6] The placement of the stapler across the smaller segmental branches of the pulmonary artery is difficult and dangerous, especially as the rather large, rigid stapler legs must pass around the tiny vessels.[4] The use of stapling devices is expensive and time-consuming because several reloadable cartridges must be used, especially for upper lobectomies. LigaSure is a bipolar vessel-sealing device proved to be effective and safe for closure of systemic arteries up to 7 mm in diameter, and is accepted in general surgery.[7-9] The company states that this technology can fuse vessels up to and including 7 mm, lymphatics, tissue bundles, and pulmonary vasculature.[10] However, the safety and efficacy of the LigaSure device remain unclear in thoracic surgery.

Our study shows that use of the LigaSure device does not result in complete fusion of all vessel wall layers, which causes a mean burst pressure of 156 mm Hg in pulmonary arteries >5 mm in diameter that is 6.4-fold less than after ligation. This is important, because 150 mm Hg was previously considered as the critical pressure for the evaluation of the sealing-system effects on pulmonary vessels.[11] In their experimental study on pigs, Santini and colleauges[11] noted that the burst pressures of pulmonary arteries with a diameter of 1-7 mm were higher than the critical pressure, but there was no declaration of absolute values. Furthermore, among pulmonary arteries sealed in vivo in sheep, Lacin and associates[4] described a dehiscence rate of 33%

TABLE 1. Patients characteristics

Characteristic	LS-PA group, n	L-PA group, n
Patients	30	30
Male/female	18/12	21/9
Age, y (range)	67 (53-79)	70 (45-87)
Resected lobe	32	31
Right	18	21
Upper	9	12
Middle	2	4
Lower	7	5
Left	14	10
Upper	8	6
Lower	6	4
Histology		
Adenocarcinoma	16	19
Squamous cell carcinoma	9	5
Carcinoid	0	2
Adenosquamous	4	1
Large-cell carcinoma	1	3
Pathologic stage		
Stage I A/B	18	14
Stage II A/B	8	9
Stage III A	4	7
Divided pulmonary arteries		
Right		
A1,3	3	3
A1	2	1
A3	0	1
A2	2	1
A5	0	1
A4,5	2	3
A6	4	5
A7,8	2	2
A9,10	2	3
Left		
A1,3	2	2
A1	1	1
A3	1	1
A2	1	1
A4	2	0
A5	0	1
A4,5	1	0
A6	3	2
A8,9	2	2

LS-PA, LigaSure–pulmonary artery; *L-PA*, suture-ligated–pulmonary artery.

with a mean pulmonary pressure of 18 mm Hg, which was a result of thermal necrosis of the vessel wall. In their study, hemorrhage occurred in pulmonary arteries >9 mm in diameter. In a study on human pulmonary arteries, Tsunezuka and colleauges[12] noted that the burst pressure was 607 mm Hg for arteries <5 mm, and 447 mm Hg for arteries >5 mm in diameter. The higher burst pressures in comparison with our results may be caused by ex vivo sealing of the resected lung lobe. Furthermore, the diameters of pulmonary arteries are not comparable. The diameter of collapsed vessels ex vivo is greater than when under perfusion. In addition,

FIGURE 2. *Box* plot with mean burst pressures of sealed (LS-PA; n = 15) and ligated pulmonary arteries (L-PA; n = 15) of different diameters (3-5 mm and 6-8 mm). The differences between sealed and ligated arteries of the same diameter are significant (LS-PA 3-5 mm vs L-PA 3-5 mm, $P < .001$; LS-PA 6-8 mm vs L-PA 6-8 mm, $P < .001$). The differences between the diameters of sealed and ligated arteries are also significant (LS-PA 3-5 mm vs LS-PA 6-8 mm, $P < .001$; L-PA 3-5 mm vs L-PA 6-8 mm, $P = .001$). *L-PA*, Suture-ligated–pulmonary artery; *LS-PA*, LigaSure–pulmonary artery.

the velocity of the pressure increase during injection into the arterial lumen could also cause different burst pressures, and in our study we increased the pressure continuously by 1 mm Hg/second. The results of the clinical part of the study of Tsunezuka and colleagues,[12] which assessed the safety of LigaSure for sealing pulmonary vessels, are only of limited use. Most of the segmental pulmonary arteries >5 mm in diameter were divided with LigaSure after ligation of the proximal sites with a suture during videothoracoscopic

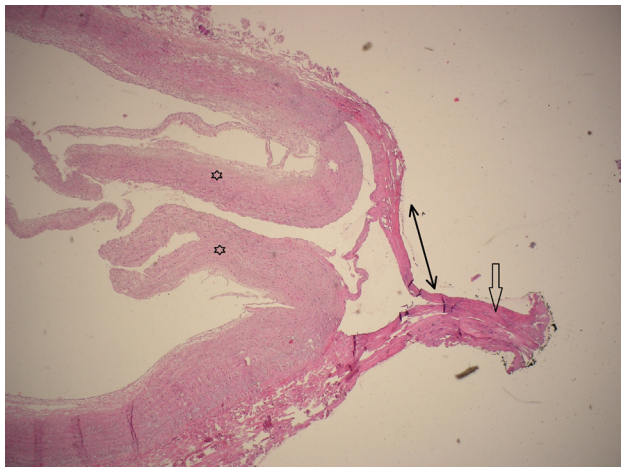

FIGURE 3. Histological section of a pulmonary artery sealed with LigaSure (hematoxylin–eosin stain, ×100). The intima and media are replaced and invaginated into the vessel lumen (*stars*). Between the sealed zone (*arrow*) and the normal vessel wall there is a vulnerable wall section that consists exclusively of adventitia (*double-headed arrow*).

lobectomy. This method could be the result of a case in which the authors describe a bleed 20 minutes after sealing a pulmonary artery 7 mm in diameter, which was not ligated with a suture in addition to the central site.

A porcine study using the harmonic scalpel showed that this device divides reliably pulmonary vessels $\leq$4 mm. However, vessels >5 mm in diameter were not tested.[13]

We found no leakage over a mean period of 32 minutes after sealing while the lung was being ventilated. It must be borne in mind that the pulmonary artery pressure is very low in the upper lung in patients in the lateral decubitus position. As such, the burst pressure measurements and the histologic examinations seem to be more important when estimating safety. For instance, by histopathology we demonstrated a vulnerable section of vessel wall that consisted exclusively of adventitia, whereas the intima and media were replaced and invaginated without fusion. More important, these findings were demonstrable in all histologic examinations. This could be caused by the specialized nature of the pulmonary vascular microscopic anatomy, in that pulmonary arteries >3 mm in diameter are among the arteries characterized by strong elastic fibers and moderately developed muscle layers.[14] Because LigaSure is closed with a defined pressure, this pressure could be too high, resulting in crushing of the vessel wall. Despite the vulnerable vessel wall, rupture occurs only from 156 mm Hg on 6 to 8-mm vessels. The bursting pressures are higher than normal pulmonary artery pressure, and are higher than those seen in patients with pulmonary hypertension. It remains unclear whether these burst pressures are low enough to create a clinical risk of rupture. In our practice, we have decided, based on these data, that it is not worth the risk to use LigaSure on pulmonary vessels unless there is a chronic survival animal model to evaluate the histologic changes over time.

Our data on pulmonary arteries differ from systemic vessels. In a experimental study of systemic arteries that were harvested from freshly euthanized pigs, Harold and coworkers[15] compared the burst pressure and histologic findings of arteries sealed with ultrasonic coagulating shears, an electrothermal bipolar vessel sealer, and laparoscopic clips. The LigaSure mean burst pressure of systemic arteries was—at 4 to 5 mm (601 mm Hg) and 6 to 7 mm (442 mm Hg)—2-fold higher than our measurements on pulmonary arteries of comparable size. Histopathologically, Harold and coworkers[15] found a complete fusion of the vessel walls. The reason might be the thicker muscle layer and a larger amount of collagenous fibers in the wall of systemic arteries.

Limitations

Limitations of this study include the small observation time of sealed pulmonary arteries in vivo. The pulmonary artery pressure during thoracotomy in the lateral decubitus position is not comparable with the pressure postoperatively if the patient moves and coughs.

CONCLUSIONS

LigaSure does not result in complete fusion of the wall layers of pulmonary arteries. The pulmonary artery burst pressure after sealing is significantly less compared with conventional suture ligation. It remains unclear whether these findings create a clinical risk of rupture.

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